WEST Search History

DATE: Saturday, October 19, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L29	L28 and (arthritis or fas or anti-fas or antifas).clm.	19	L29
L28	L27 and @ad<20011120	211	L28
L27	L26 and ((fas or anti-fas or antifas) with antibody)	217	L27
L26	($trexate or epiroprim or iometrexol or pyritexim or brodimoprim or MX-68) and (rheumatoid adj arthritis)	2566	L26
L25	(l22 or l24) and (rheum$ with arthrit$)	1	L25
L24	L23 not l9	3	L24
L23	($trexate or epiroprim or iometrexol or pyritexim or brodimoprim or MX-68) same (((anti-fas or antifas or fas or apoptosis) with induc$) with antibody)	6	L23
L22	L21 not l9	4	L22
L21	($trexate or epiroprim or iometrexol or pyritexim or brodimoprim or MX-68) same (anti-fas or antifas or ((fas or apoptosis) with induc$) with antibody)	8	L21
L20	L19 not l9	13	L20
L19	L18 and l12	15	L19
L18	L17 and ($trexate or epiroprim or iometrexol or pyritexim or brodimoprim or MX-68)	730	L18
L17	L15	1146	L17
L16	L15	1146	L16
L15	L14 and @ad<20011120	1146	L15
L14	(folate or dihydrofolate) and (rheum$ with arthrit$)	1192	L14
L13	(foalte or dihydrofolate) and (rheum$ with arthrit$)	1002	L13
L12	l10 and (rheum$ with arthrit$)	98	L12
L11	l10 and l7	4	L11
L10	(anti-fas or antifas) with antibody	313	L10
L9	L7 and l1	6	L9
L8	L7 and l3	4	L8
L7	antibody same (folate or dihydrofolate)	655	L7
L6	L5 and @ad<20011120	40	L6
L5	L3 and antibody same apoptosis	41	L5
L4	L3 and antibody same apotosis	0	L4
L3	L1 and (anti-fas or antifas) with antibody	47	L3
L2	[illegible]	0	L2

L2	L1 and (antifas or antifas) with antibody	0	L2
L1	(anti-fas or antifas) and (folate or dihydrofolate)	52	L1

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DATE: Saturday, October 19, 2002 Printable Copy Create Case

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L2	L1 and (antifas or antifas) with antibody	0	L2
L1	(anti-fas or antifas) and (folate or dihydrofolate)	52	L1

END OF SEARCH HISTORY

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L22: Entry 3 of 4 File: USPT Jan 9, 2001

DOCUMENT-IDENTIFIER: US 6172190 B1
TITLE: Caspase-8h and Caspase-8i-polypeptides

Detailed Description Text (21):
Numerous substances, in addition to the anti-Fas antibody described above, are capable of inducing apoptosis in various cell types and can thus be used in assays of apoptosis. These substances include physiological activators, such as TNF family members, TGF-.beta., the neurotransmitters glutamate, dopamine, and NMDA (N-methyl-D-aspartate), calcium, and glucocorticoids. Cell death can also be induced when growth factors are withdrawn from the medium in which the cells are cultured. Additional inducers of apoptosis include heat shock, viral infection, bacterial toxins, expression of the oncogenes myc, rel, and E1A, expression of tumor suppressor genes, cytolytic T cells, oxidants, free radicals, gamma and ultraviolet irradiation, .beta.-amyloid peptide, ethanol, and chemotherapeutic agents such as Cisplatin, doxorubicin, arabinoside, nitrogen mustard, methotrexate, and vincristine.

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L29: Entry 12 of 19 File: USPT Oct 8, 2002

DOCUMENT-IDENTIFIER: US 6462041 B1
TITLE: Gambogic acid, analogs and derivatives as activators of caspases and inducers of apoptosis

DATE FILED (1):
20000203

Brief Summary Text (10):
It has been shown that chemotherapeutic (anti-cancer) drugs can trigger cancer cells to undergo suicide by activating the dormant caspase cascade. This may be a crucial aspect of the mode of action of most, if not all, known anticancer drugs (Los et al., Blood, Vol. 90, No 8:3118-3129 (1997); Friesen, et al., Nat. Med. 2:574 (1996)). The mechanism of action of current antineoplastic drugs frequently involves an attack at specific phases of the cell cycle. In brief, the cell cycle refers to the stages through which cells normally progress during their lifetimes. Normally, cells exist in a resting phase termed G.sub.o. During multiplication, cells progress to a stage in which DNA synthesis occurs, termed S. Later, cell division, or mitosis occurs, in a phase called M. Antineoplastic drugs such as cytosine arabinoside, hydroxyurea, 6-mercaptopurine, and methotrexate are S phase specific, whereas antineoplastic drugs such as vincristine, vinblastine, and paclitaxel are M phase specific. Many antineoplastic drugs slow growing tumors. For example, colon cancers exist -primarily in the G.sub.o phase, whereas rapidly proliferating normal tissues, for example bone marrow, exist primarily in the S or M phase. Thus, a drug like 6-mercaptopurine can cause bone marrow toxicity while remaining ineffective toward a slow growing tumor. Other aspects of the chemotherapy of neoplastic diseases are known to those skilled in the art (see, e.g., Hardman, et al., eds., Goodman and Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition, McGraw-Hill, New York (1996), pp. 1225-1287). Thus, it is clear that the possibility exists for the activation of the caspase cascade, although the exact mechanisms for doing so are not clear at this point. It is equally clear that insufficient activity of the caspase cascade and consequent apoptotic events are implicated in various types of cancer. The development of caspase cascade activators and inducers of apoptosis is a highly desirable goal in the development of therapeutically effective antineoplastic agents. Moreover, since autoimmune diseases and certain degenerative diseases also involve the proliferation of abnormal cells, therapeutic treatment for these diseases could also involve the enhancement of the apoptotic process through the administration of appropriate caspase cascade activators and inducers of apoptosis.

Detailed Description Text (49):
Another embodiment of the present invention is directed to a composition effective to inhibit neoplasia comprising a compound, or a pharmaceutically acceptable salt or prodrug of said compound of Formulae I-III, which functions as a caspase cascade activator and inducer of apoptosis, in combination with at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent. Examples of known anti-cancer agents which can be used for combination therapy include, but are not limited to, alkylating agents such as busulfan, cis-platin, mitomycin C, and carboplatin; antimitotic agents such as colchicine, vinblastine, paclitaxel, and docetaxel; topo I inhibitors such as camptothecin and topotecan; topo II inhibitors such as doxorubicin and etoposide; RNA/DNA antimetabolites such as 5-azacytidine, 5-fluorouracil and methotrexate; DNA antimetabolites such as 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea and thioguanine; antibodies such as Herceptin.RTM. (trastuzumab) and Rituxan.RTM. (rituximab). Other known anti-cancer agents which can be used for combination therapy include melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen and alanosine.

Detailed Description Text (57):
Bisindolylmaleimide VIII is known to potentiate Fas-mediated apoptosis in human astrocytoma 1321N1 cells and in Molt-4T cells, and both of which were resistant to apoptosis induced by anti-Fas antibody in the absence of bisindolylmaleimide VIII. Potentiation of Fas-mediated apoptosis by bisindolylmaleimide VIII was reported to be selective for activated, rather than non-activated, T cells, and was Fas-dependent. Zhou T. et al. (Nat Med 5(1):42-8 (1999)) reported that administration of bisindolylmaleimide VIII to rats during autoantigen stimulation prevented the development of symptoms of T cell-mediated autoimmune diseases in two models: the Lewis rat model of experimental allergic encephalitis and the Lewis adjuvant arthritis model. Therefore, the application of a Fas-dependent apoptosis enhancer such as bisindolylmaleimide VIII may be therapeutically useful for the more effective elimination of detrimental cells and inhibition of T cell-mediated autoimmune diseases. Therefore, an effective amount of a compound, or a pharmaceutically acceptable salt or prodrug of the compound of Formulae I-III, which functions as a caspase cascade activator and inducer of apoptosis, should be an effective treatment for autoimmune disease.

Detailed Description Text (58):
Psoriasis is a chronic skin disease which is characterized by scaly red patches. Psoralen plus ultraviolet A (PUVA) is a widely used and effective treatment for psoriasis vulgaris. Coven, et al., Photodermatol Photoimmunol Photomed 15(1):22-7 (1999), reported that lymphocytes treated with psoralen 8-MOP or TMP plus UVA displayed DNA degradation patterns typical of apoptotic cell death. Ozawa, et al., J. Exp. Med 189(4):711-718 (1999) reported that induction of T cell apoptosis could be the main mechanism by which 312-nm UVB resolves psoriasis skin lesions. Low doses of methotrexate may be used to treat psoriasis to restore a clinically normal skin. Heenen, et al., Arch. Dermatol. Res. 290(5):240-245 (1998), reported that low doses of methotrexate may induce apoptosis and this mode of action could explain the reduction in epidermal hyperplasia during treatment of psoriasis with methotrexate. Therefore, an effective amount of a compound, or a pharmaceutically acceptable salt or prodrug of the compound of Formulae I-III, which functions as a caspase cascade activator and inducer of apoptosis, should be an effective treatment for psoriasis.

Detailed Description Text (59):
Synovial cell hyperplasia is a characteristic of patients with rheumatoid arthritis (RA). Excessive proliferation of RA synovial cells as well as defects in synovial cell death may be responsible for synovial cell hyperplasia. Wakisaka, et al., Clin. Exp. Immunol. 114(1):119-28 (1998), found that although RA synovial cells could die via apoptosis through Fas/FasL pathway, apoptosis of synovial cells was inhibited by proinflammatory cytokines present within the synovium. This suggested that inhibition of apoptosis by the proinflammatory cytokines may contribute to the outgrowth of synovial cells, and lead to pannus formation and the destruction of joints in patients with RA. Therefore, an effective amount of a compound, or a pharmaceutically acceptable salt or prodrug of the compound of Formulae I-III, which functions as a caspase cascade activator and inducer of apoptosis, should be an effective treatment for RA.

Detailed Description Text (244):
Identification Of Vinblastine, Cisplatin, 5-Fluorouracil, Taxol, Camptothecin, Doxorubicin, Etoposide And Methotrexate As Conventional Antineoplastic Agents That Are Not Efficient Caspase Cascade Activators In Solid Tumors

Detailed Description Text (250):
Thus, vinblastine, cisplatin, 5-fluorouracil, taxol, camptothecin, doxorubicin, etoposide and methotrexate are identified as known antineoplastic compounds that are not caspase cascade activators in this assay.

Detailed Description Paragraph Table (4):
TABLE IV Activity of Known Antineoplastic Compound as Caspase Cascade Activators
Cell lines T-47D PC-3 Vinblastine 0.9 0.8 Cisplatin 1.1 0.9 5-fluorouracil 0.8 0.7 Taxol 0.9 0.7 Camptothecin 0.7 0.6 Doxorubicin 1.3 1.1 Etoposide 1.0 0.8 Methotrexate 0.8 0.7

Other Reference Publication (21):
Heenen, M. et al., " Methotrexate induces apoptotic cell death in human keratinocytes," Arch. Dermatol. Res. 290:240-245 (1998).

Other Reference Publication (41):
Wakisaka, S. et al., "Modulation by proinflammatory cytokines of Fas.Fas ligand-mediated apoptotic cell death of synovial cells in patients with rheumatoid arthritis (RA)," Clin. Exp. Immunol. 114:119-128 (1998).

CLAIMS:

14. The method according to claim 13, wherein said known cancer chemotherapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin.RTM. (trastuzumab), Rituxan.RTM. (rituximab) and alanosine.

18. The method according to claim 1, wherein the mammal has rheumatoid arthritis .

35. The pharmaceutical composition of claim 34, wherein said known cancer chemotherapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, caiptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, meiphalan, chorambucil, cyclophosamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin.RTM. (trastuzumab), Rituxan.RTM. (rituximab) and alanosine.